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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,082	11/13/2003	Bettina Moeckel	245266US0X CONT	7284

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,082	MOECKEL ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment canceling claims 1-87 and adding new claims 88-104 and amending the specification, in the paper of 4/19/2004, is acknowledged. Claims 88-104 are at issue and are present for examination.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of the information disclosure statement, filed on 11/13/2003, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities: Applicants amendment of the specification on 4/19/2004 at page 1 which states "U.S. Application No. 10/076,406, filed February 19,2002 (now allowed)..." is objected to because this parent application is not allowed, but rather it is abandoned.

Appropriate correction is required.

Claim Objections

Claims 88 are objected to because of the following informalities:

Claim 88 states "...in an medium suitable...". This should be "...in **a** medium suitable...".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 88-104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 88 (claims 89-104 dependent on) is indefinite in the recitation "...the unmodified starting strain...", because there is no antecedent basis for "the unmodified starting strain". It is noted that as there is no antecedent basis for the recited "unmodified starting strain, and there is no active step in the claim that requires the modification of a "starting strain", the claim is interpreted as broadly as is reasonable, as being drawn to the use of any coryneform bacterium which expresses an increased amount of the product of the rpoB gene relative to any strain.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88-104 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 88-104 are directed to all possible processes for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid, by fermentation and recovering said L-amino acid (See above 112 second paragraph rejection). There is no disclosure of any particular structure to function/activity relationship for the claimed genus of methods nor are there examples of the multitude of methods encompassed in the claimed method. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 88-104 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for making an L-amino acid comprising

culturing a coryneform bacterium which has been transfected with a nucleic acid comprising SEQ ID NO: 1, which encodes the β-subunit of RNA polymerase B and overexpressing said nucleic acid and culturing said strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid, does not reasonably provide enablement for any processes for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5 are so broad as to encompass any processes for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid by fermentation and recovering

said L-amino acid. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methods and processes broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place insufficient structural and no functional means/limits on the claimed processes. Since the sequence of a nucleic acid and protein determines its structural and functional properties, predictability of which changes can be tolerated in a sequence and obtain the desired activity (i.e. an increase in expression) requires a knowledge of and guidance with regard to which positions in the sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the sequence relates to its function. However, in this case the disclosure is limited to a process for making an L-amino acid comprising culturing a coryneform bacterium which has been transfected with a nucleic acid comprising SEQ ID NO: 1, which encodes the β-subunit of RNA polymerase B and overexpressing said nucleic acid and culturing said strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid, does not reasonably provide enablement for any processes for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the

instant claims, and the positions within a polynucleotide or amino acid sequence where modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide or protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given polynucleotide to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any process for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid, because the specification does not establish: (A) regions of the polynucleotide and protein structure which may be modified to bring about the desired activity (i.e. increased expression); (B) the general tolerance of the recited polynucleotides and proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying the sequence of SEQ ID NO: 1 and the encoded protein with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not

predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those processes of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any processes for making an L-amino acid comprising culturing any coryneform bacterium which expresses an increased amount of the product of the rpoB gene compared to the (an) unmodified starting strain in a medium suitable for production of said L-amino acid by fermentation and recovering said L-amino acid. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those processes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax

phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
5/24/2006